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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/784,554	02/16/2001	Kirk Schnorr	10017.200-US	5362
25908	7590	12/24/2003	EXAMINER	
NOVOZYMES NORTH AMERICA, INC. 500 FIFTH AVENUE SUITE 1600 NEW YORK, NY 10110			RAO, MANJUNATH N	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/784,554

Applicant(s)

SCHNORR ET AL.

Examiner

Manjunath N. Rao, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33,35-40 and 42-71 is/are pending in the application.
- 4a) Of the above claim(s) 71 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33,35,42,48,49 and 70 is/are rejected.
- 7) ☒ Claim(s) 36-40,43-47 and 50-69 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claims 33, 35-40, 42-71 are still at issue and are present for examination. Claims 33-70 are now under consideration. Claims 33, 35-40, 42-70 are now under consideration. Claim 71 remains withdrawn from consideration as being drawn to non-elected invention.

Applicants' amendments and arguments filed on 10-10-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33, 35, 42, 48-49, 70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a xyloglucanase enzyme with SEQ ID NO:2, 4, or 6 and encoded by the polynucleotide with SEQ ID NO:1, 3 or 5, does not reasonably provide enablement for any xyloglucanase that is either 80%, 85%, 90%, identical to amino acids 36-559 or 40-559 of SEQ ID NO:2, 4, or 6 or such a polypeptide encoded by a DNA sequence that hybridizes to nucleotides 121-1677 of SEQ ID NO:1, 3, including mutants, variants and recombinants isolated from any source or any xyloglucanase isolated from any microorganism including fungi, bacteria such as gram positive bacteria, bacteria belonging to *Bacillus/Lactobacillus* subdivision, *Paenibacillus* sp. or any strain of *P.polymyxa* and yeasts. The specification does not enable any person skilled in the art to which it pertains, or with which

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it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 33, 35, 42, 48-49, 70 are so broad as to encompass any xyloglucanase isolated from any source including variants, mutants and recombinants having 80%, 85%, 90%, identical to amino acids 36-559 or 40-559 of SEQ ID NO:2, 4, or 6. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of xyloglucanases (including mutants, variants and recombinants) broadly encompassed by these claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of only 3 enzymes (i.e., SEQ ID NO:1, 3, and 5).

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In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in *The Protein Folding Problem and Tertiary Structure Prediction*, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all xyloglucanases (as indicated above) and modifications and fragments of any xyloglucanase from any given source because the specification does not establish: (A) a rational and predictable scheme for isolation of the enzyme from any source; (B) regions of the protein structure which may be modified without effecting its activity; (C) the general tolerance of xyloglucanases to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any xyloglucanase amino acid residues with an expectation of obtaining the desired biological

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function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including all or any xyloglucanase isolated from any source including mutants, variants and recombinants with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of xyloglucanases having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicants have amended the claims to limit the scope of claimed xyloglucanases and argued against the above rejection. However, Examiner continues to maintain the above rejection in view of the claim amendments for reasons presented above as the amended claims still encompass many xyloglucanases with a large number of modifications which would require undue experimentation to make, based on the limited guidance provided by the three disclosed xyloglucanases. Applicants argue that the rejection under 35 U.S.C. §112, first paragraph is not proper because the specification teaches the complete nucleotide and amino acid sequences of the claimed enzymes and polynucleotides, protocols for using the polynucleotide, and protocols for testing for enzymatic activity, and methods for producing variants of a disclosed sequence are within the skill of the ordinary artisan. This is not persuasive because while methods to produce variants of a known sequence

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such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan producing variants as claimed by applicants (i.e., a polynucleotide with specific % homology and capable of encoding xyloglucanase) requires that one of ordinary skill in the art know or be provided with guidance for making the changes required and the selection of which of the infinite number of variants have the claimed property. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute undue experimentation. Even though applicants argue that their specification does provide such guidance, Examiner takes the position that such guidance is still insufficient as applicants have not specifically taught as to where exactly one can make the changes while retaining in the property of the polynucleotide to encode the xyloglucanase. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) a rational and predictable scheme for isolation of the enzyme from any source; (B) regions of the protein structure which may be modified without effecting its activity; (C) the general tolerance of xyloglucanases to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any xyloglucanase amino acid residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Conclusion

Claims 36-40, 43-47, 50-69 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.


THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.


MANJUNATH N. RAO
PATENT EXAMINER

Manjunath N. Rao, Ph.D.
Patent Examiner, A.U. 1652
December 22, 2003